

### **Amendments to the Claims**

This listing will replace all prior versions of the claims, and the prior listing of claims in the application:

1. (Currently amended) A method of inhibiting angiogenesis ~~or tumorigenesis~~ in a biological sample, comprising
  - a. providing a biological sample; and
  - b. combining the biological sample with an angiogenesis-inhibiting ~~or tumorigenesis-inhibiting~~ amount of a composition comprising an inhibitor of apelin activity.
2. (Original) The method of Claim 1, wherein the composition decreases vascular permeability in the biological sample.
3. (Original) The method of Claim 1, wherein the composition interferes with the interaction of an apelin polypeptide or apelin peptide with a receptor polypeptide.
4. (Original) The method of Claim 1, wherein the composition interferes with the interaction of an apelin polypeptide or apelin peptide with APJ.
5. (Original) The method of Claim 1, wherein the composition further comprises an anti-cancer agent and wherein the anti-cancer agent is selected from the group consisting of a chemotherapeutic agent, a radiotherapeutic agent, an anti-angiogenesis agent, and an apoptosis-inducing agent.
6. (Currently amended) The method of Claim 5, wherein the composition comprises an anti-angiogenesis agent that inhibits an angiogenic factor selected from the group consisting of VEGF (VEGF-A), VEGF-B, VEGF-C, VEGF-D, VEGF-E, PlGF, acidic fibroblast growth factor (FGF-1), basic fibroblast growth factor (FGF-2), VEGFs, FGFs, PDGFB, EGF, LPA, HGF, PD-ECF, IL-8, angiogenin, TNF-alpha, TGF-beta, TGF-alpha, proliferin, and PLGF.

7. (Original) The method of Claim 1, wherein the composition comprises an anti-apelin antibody or fragment thereof.
8. (Currently amended) The method of Claim 7, wherein the antibody or fragment thereof binds a polypeptide that is selected from the group consisting of:
  - a. a polypeptide as defined in SEQ ID NO:1;
  - b. a polypeptide as defined in SEQ ID NO:2;
  - c. a polypeptide as defined in SEQ ID NO:3;
  - d. a polypeptide as defined in SEQ ID NO:4; and
  - e. a polypeptide as defined in SEQ ID NO:5; and
  - ~~f. a polypeptide having at least 80% sequence identity with the polypeptide of a) through e) above.~~
9. (Original) The method of Claim 7, wherein the antibody or fragment thereof binds the polypeptide of SEQ ID NO:1.
10. (Original) The method of Claim 7, wherein the antibody or fragment thereof binds the polypeptide of SEQ ID NO:2.
11. (Original) The method of Claim 7, wherein the antibody or fragment thereof binds the polypeptide of SEQ ID NO:3.
12. (Original) The method of Claim 7, wherein the antibody or fragment thereof binds the polypeptide of SEQ ID NO:4.
13. (Original) The method of Claim 7, wherein the antibody or fragment thereof binds the polypeptide as defined in SEQ ID NO:5.
14. (Canceled)
15. (Withdrawn) The method of Claim 1, wherein the inhibitor of apelin activity is an anti-APJ antibody or fragment thereof.

16. (Withdrawn) The method of Claim 15, wherein the antibody or fragment thereof binds a polypeptide as defined in SEQ ID NO:17.

17. (Canceled)

18. (Withdrawn) The method of Claim 1, wherein the inhibitor of apelin activity is selected from the group consisting of an apelin antisense nucleic acid, receptor decoy, ribozyme, sense polynucleotide, double stranded RNA, RNAi, aptamer, and small molecule antagonist.

19. (Withdrawn) The method of Claim 1, wherein the inhibitor of apelin activity is selected from the group consisting of an APJ antisense nucleic acid, receptor decoy, ribozyme, sense polynucleotide, double stranded RNA, RNAi, aptamer, and small molecule antagonist.

20. (Withdrawn) The method of Claim 1, wherein the inhibitor of apelin activity is an inhibitor of a serine protease that cleaves a polypeptide specifically after an arginine residue.

21. (Original) The method of Claim 1, wherein the composition comprises a pharmaceutically acceptable carrier.

22. (Currently amended) The method of Claim 1, wherein the biological sample is a mammalian biological sample ~~from a mammal~~.

23. (Original) The method of Claim 1, wherein the biological sample is a human biological sample.

24. (Original) The method of Claim 23, wherein the biological sample is in a patient.

25. (Original) The method of Claim 24, wherein the composition is introduced by a route selected from the group consisting of subcutaneous injection, intravenous injection, intraocular injection, intradermal injection, intramuscular injection, intraperitoneal injection, intratracheal administration, epidural administration, inhalation, intranasal administration, oral administration, sublingual administration, buccal administration, rectal administration, vaginal administration, and topical administration.

26. (Currently amended) The method of Claim 24, wherein the patient has a disease or condition involving angiogenesis ~~or tumorigenesis~~.

27. (Canceled)

28. (Currently amended) The method of Claim 24, further comprising

- c. administering to the patient a therapeutically effective amount of an anti-cancer agent,

wherein the anti-cancer agent is selected from the group consisting of a chemotherapeutic agent, a radiotherapeutic agent, an anti-angiogenic agent, and an apoptosis-inducing agent.

29. (Original) The method of Claim 28, wherein the anti-cancer agent is an anti-angiogenic agent.

30. (Currently amended) The method of Claim 28, wherein the anti-angiogenic agent is an inhibitor of an angiogenic factor selected from the group consisting of VEGF (VEGF-A), VEGF-B, VEGF-C, VEGF-D, VEGF-E, PlGF, acidic fibroblast growth factor (FGF-1), basic fibroblast growth factor (FGF-2), VEGFs, FGFs, PDGFB, EGF, LPA, HGF, PD-ECF, IL-8, angiogenin, TNF-alpha, TGF-beta, TGF-alpha, proliferin, and PLGF.

31.-59. (Canceled)